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499

Access DB# 76303

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: PATEL SUDHAKER Examiner #: 77016 Date: 9/23/02

Art Unit: 1624 Phone Number 30 8 4709 Serial Number: 09/895,843

Mail Box and Bldg/Room Location: CM1 4E17 Results Format Preferred (circle): PAPER DISK E-MAIL

4E12

If more than one search is submitted, please prioritize searches in order of need.

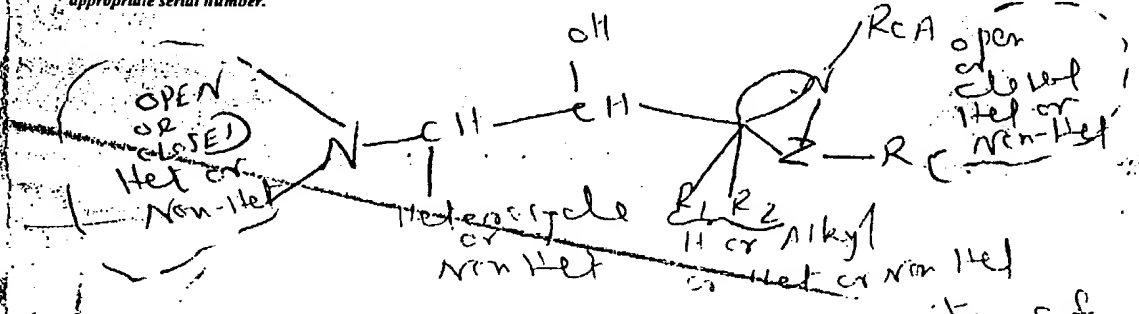
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: COMPOUNDS TO TREAT ALZHEIMER'S DISEASE

Inventors (please provide full names): JAMES P. Beck et al

Earliest Priority Filing Date: 6/30/2000

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*



Need info @ compounds, compositions & method of treating ALZHEIMER'S Disease

copy of claims endorsed

Point of Contact:
Barb O'Bryen
Technical Information Specialist
STIC CM1 6A05 308-4291

THX

Need db hits

STAFF USE ONLY

Searcher: BOB

Searcher Phone #:

Searcher Location:

Date Searcher Picked Up:

Date Completed: 9-26-02

Searcher Prep & Review Time: 90

Clerical Prep Time:

Online Time: 35

Type of Search

NA Sequence (#)

AA Sequence (#)

Structure (#) 2

Bibliographic

Litigation

Fulltext

Patent Family

Other

Vendors and cost where applicable

STN 520

Dialog

Questel/Orbit

Dr.Link

Lexis/Nexis

Sequence Systems

WWW/Internet

Other (specify) Chem Draw

PTO-1590 (8-01)

Welcome to STN International! Enter x:x

LOGINID:ssspta1611sxp

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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS	4	Jul 15	Data from 1960-1976 added to RDISCLOSURE
NEWS	5	Jul 21	Identification of STN records implemented
NEWS	6	Jul 21	Polymer class term count added to REGISTRY
NEWS	7	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS	8	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS	9	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS	10	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS	11	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS	12	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS	13	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS	14	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS	15	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS	16	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS	17	AUG 18	Simultaneous left and right truncation added to ANABSTR

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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Patel 9/20/2003>

FILE 'HOME' ENTERED AT 12:32:13 ON 20 SEP 2003

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 12:32:24 ON 20 SEP 2003
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STRUCTURE FILE UPDATES: 18 SEP 2003 HIGHEST RN 588668-76-2
DICTIONARY FILE UPDATES: 18 SEP 2003 HIGHEST RN 588668-76-2

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

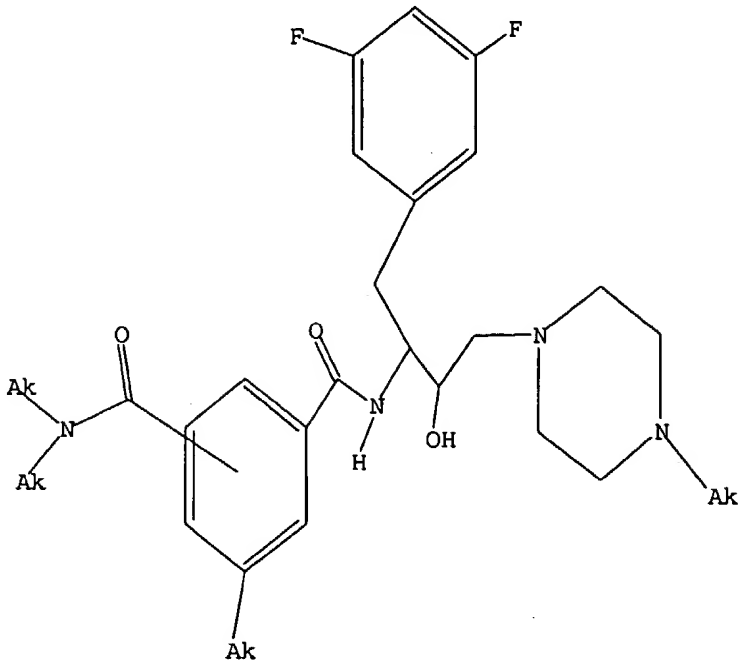
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09895843.1

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 12:32:45 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      7 TO ITERATE

100.0% PROCESSED       7 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            7 TO      298
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 12:32:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    103 TO ITERATE

100.0% PROCESSED     103 ITERATIONS                             3 ANSWERS
SEARCH TIME: 00.00.01

L3            3 SEA SSS FUL L1

=> file marpat
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY     SESSION
FULL ESTIMATED COST                           148.95     149.16
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Patel 9/20/2003>

FILE 'MARPAT' ENTERED AT 12:34:23 ON 20 SEP 2003
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FILE CONTENT: 1988-PRESENT (VOL 104 ISS 15-VOL 139 ISS11)(20030912ED)

MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 6605638 12 AUG 2003
DE 20300703 07 AUG 2003
EP 1335416 13 AUG 2003
JP 2003230397 19 AUG 2003
WO 2003068205 21 AUG 2003

Structure search limits have been raised. See HELP SLIMIT for the new, higher limits.

=> s l1 sss full
FULL SEARCH INITIATED 12:34:32 FILE 'MARPAT'
FULL SCREEN SEARCH COMPLETED - 925 TO ITERATE

100.0% PROCESSED 925 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.04

L4 2 SEA SSS FUL L1

=> d l4 fbib hitstr abs total
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'MARPAT'

The following are valid formats:

MSTR ----- All Markush structure(s) and related text information
MSTR(n) -- Markush structure(n) and related text information
IDE ------ AN and MSTR

ABS ------ AB
ALL ------ BIB, AB, IND, RE, and MSTR
APPS ----- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN ------ List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
DALL ----- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND ------ Indexing Data
IPC ------ International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS ----- PI, SO
SAM ------ CC, SX, TI, ST, IT, and FQHIT
SCAN ----- CC, SX, TI, ST, IT, and FQHIT (random display, no answer numbers)
STD ------ BIB, IPC, and NCL (standard patent information)

IABS ----- ABS, indented with text labels
IALL ----- ALL, indented with text labels

```
IBIB ----- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD ----- STD, indented with text labels
OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations


HIT ------ Fields containing hit text terms and the Markush
           structures containing the query structure
FHIT ----- Fields containing the first hit text terms and the first
           Markush structures containing the query structure
QHIT ----- Fields containing query focus hit text terms and the
           Markush structures containing the query structure
FQHIT ---- Fields containing the first query focus hit text terms and
           the first Markush structures containing the query structure

To display a particular field or fields, enter the display field
codes.  For a list of the display field codes, enter "HELP DFIELDS"
at an arrow prompt (=>).  Examples of formats include: "TI";
"TI,MSTR,ABS"; "BIB,ST"; "TI,IND"; "TI,SO".  You may specify the
format fields in any order and the information will be displayed
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All of the formats (except for SAM, SCAN, FHIT, HIT, FQHIT, or QHIT) may
be used with the DISPLAY ACC command to display the record for a
specified Accession Number.
ENTER DISPLAY FORMAT (BIB):bib

L4   ANSWER 1 OF 2  MARPAT  COPYRIGHT 2003 ACS on STN
AN   136:102193  MARPAT
TI   Preparation of disubstituted amines for treating Alzheimer's disease
IN   Beck, James P.; Gailunas, Andrea; Hom, Roy; Jagodzinska, Barbara; John,
     Varghese; Maillaird, Michel
PA   Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SO   PCT Int. Appl., 286 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 5
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2002002520      A2   20020110       WO 2001-US21000  20010702
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,
             FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
             MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ,
             TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     US 2002143177      A1   20021003       US 2001-895843   20010629
     AU 2001073132      A5   20020114       AU 2001-73132    20010702
PRAI US 2000-215323P  20000630
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US 2001-895843 20010629
WO 2001-US21000 20010702

L4 ANSWER 2 OF 2 MARPAT COPYRIGHT 2003 ACS on STN
AN 136:102192 MARPAT
TI Preparation of disubstituted amines for treating Alzheimer's disease
IN Beck, James P.; Gailunas, Andrea; Hom, Roy; Jagodzinska, Barbara; John, Varghese; Maillaird, Michel
PA Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SO PCT Int. Appl., 286 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002002518	A2	20020110	WO 2001-US20856	20010629
	WO 2002002518	A3	20020808		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001073094	A5	20020114	AU 2001-73094	20010629
	US 2002016320	A1	20020207	US 2001-896874	20010629
	US 2003096864	A1	20030522	US 2001-895871	20010629
PRAI	US 2000-215323P		20000630		
	WO 2001-US20856		20010629		

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	106.87	256.03

FILE 'CAPLUS' ENTERED AT 12:35:21 ON 20 SEP 2003
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FILE COVERS 1907 - 20 Sep 2003 VOL 139 ISS 13
FILE LAST UPDATED: 19 Sep 2003 (20030919/ED)

L Number	Hits	Search Text	DB	Time stamp
1	1946	("514/252.12,616,617").CCLS	USPAT	2003/02/28 16:39
2	1315	("544/358,398,402").CCLS	USPAT	2003/02/28 16:39
3	127	(("514/252.12,616,617").CCLS) and (("544/358,398,402").CCLS)	USPAT	2003/02/28 16:39
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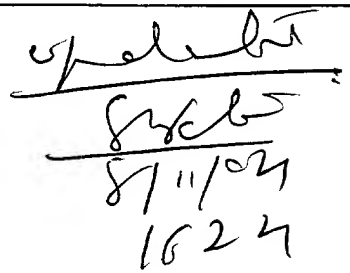

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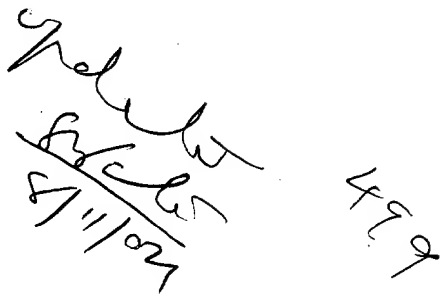

C:\APPS\EAST\bin\\default.wsp

cyclohexyl, pyridyl, pyrimidinyl, pyrazinyl, oxopyridinyl, diazinyl, triazolyl, thienyl, oxazolyl, oxadiazolyl, thiazolyl, pyrrolyl, or furyl, optionally substituted. R3 is: H, hydroxy, lower-alkoxy, or lower-alkenyloxy; R4 is: H, lower-alkyl, lower-alkenyl, lower-alkoxy, hydroxy-lower-alkyl, lower-alkoxy-lower-alkyl, benzyl, oxo, or where R3 and R4 together are a bond, or as specified in the claims. Q is: ethylene, or is absent; X is: a bond, -O-, -S-, -CH-R11- (R11 defined in claims), -CHOR9- (R9 defined in claims), -OCO, -CO-, or C:NOR10- (R10 is carboxyalkyl, alkoxycarbonylalkyl, alkyl or H), with the bond emanating from an O or S atom joining to a saturated C atom of group Z or to R1; W is: -O-, or -S-; Z is: lower-alkylene, lower-alkenylene, hydroxy-lower-alkylidene, -O-, -S-, -O-Alk- (Alk is a lower alkylene), -S-Alk-, -Alk-O-, or -Alk-S. N is: 1, or 0 or 1 when X is -O-CO; and where m is 0 or 1; with provisos.

```
=> d his

     (FILE 'HOME' ENTERED AT 13:25:08 ON 28 FEB 2004)

     FILE 'REGISTRY' ENTERED AT 13:25:18 ON 28 FEB 2004
L1              STRUCTURE UPLOADED
L2           10 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 13:25:57 ON 28 FEB 2004
L3            8 S L2
L4          234 S ALZHEIMER AND PIPERAZINE
L5            0 S L3 AND L4
L6           14 S L4 AND PREVENTING
L7           21 S L4 AND PREVENTION
L8            4 S L4 AND PREVENTION AND PREVENTING AND DISEASE

=> s l3 and alzheimer
L9            0 L3 AND ALZHEIMER

=> s l3 and prevention and preventing a disease
L10           0 L3 AND PREVENTION AND PREVENTING A DISEASE
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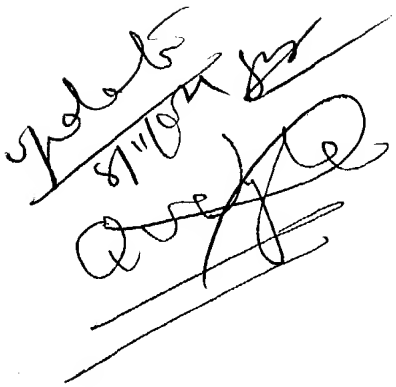

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LOGINID:ssspta1611sxp

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 4	DEC 08	INPADOC: Legal Status data reloaded
NEWS 5	SEP 29	DISSABS now available on STN
NEWS 6	OCT 10	PCTFULL: Two new display fields added
NEWS 7	OCT 21	BIOSIS file reloaded and enhanced
NEWS 8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS 9	NOV 24	MSDS-CCOHS file reloaded
NEWS 10	DEC 08	CABA reloaded with left truncation
NEWS 11	DEC 08	IMS file names changed
NEWS 12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS 13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS 14	DEC 17	DGENE: Two new display fields added
NEWS 15	DEC 18	BIOTECHNO no longer updated
NEWS 16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS 17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS 18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 19	DEC 22	ABI-INFORM now available on STN
NEWS 20	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 22	FEB 05	German (DE) application and patent publication number format changes

NEWS EXPRESS	DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:25:08 ON 28 FEB 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:25:18 ON 28 FEB 2004
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STRUCTURE FILE UPDATES: 27 FEB 2004 HIGHEST RN 655785-05-0
DICTIONARY FILE UPDATES: 27 FEB 2004 HIGHEST RN 655785-05-0

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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Uploading c:\program files\stnexp\queries\09895843.5

L1 STRUCTURE UPLOADED

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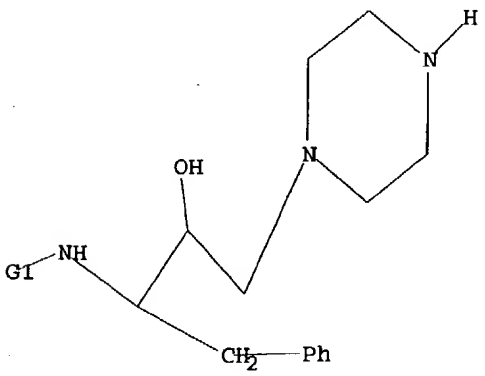
L1 HAS NO ANSWERS
L1 STR



G1 H,Cb,Cy,Ak

Structure attributes must be viewed using STN Express query preparation.

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FULL SCREEN SEARCH COMPLETED -    498 TO ITERATE

100.0% PROCESSED     498 ITERATIONS                          10 ANSWERS
SEARCH TIME: 00.00.01

L2            10 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               155.42     155.63

FILE 'CAPLUS' ENTERED AT 13:25:57 ON 28 FEB 2004
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COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



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FILE COVERS 1907 - 28 Feb 2004  VOL 140 ISS 10
FILE LAST UPDATED: 27 Feb 2004  (20040227/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s l2
L3            8 L2

=> d l3 fbib hitstr abs total

L3   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2001:468210  CAPLUS
DN   135:61557
TI   Preparation of amino acid derivatives as retroviral protease inhibitors
IN   Chen, Xiaoqi; Kempf, Dale J.; Norbeck, Daniel W.
PA   Abbott Laboratories, USA
SO   U.S., 24 pp.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
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PI US 6251906 B1 20010626 US 1999-309141 19990510
US 1998-85709P P 19980515
US 2001008892 A1 20010719 US 2001-777282 20010206
US 1998-85709P P 19980515
US 1999-309141 A319990510

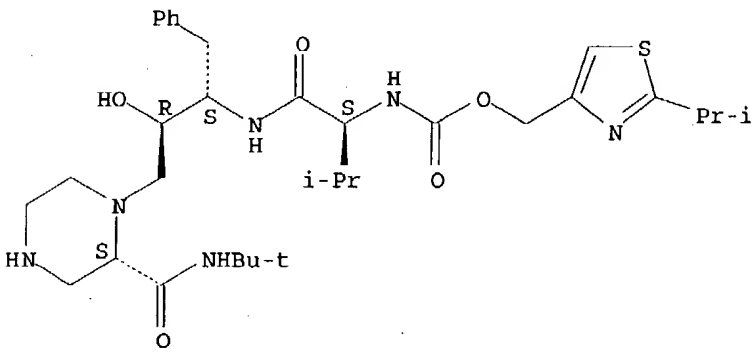
OS MARPAT 135:61557

IT **251105-64-3P 251105-79-0P 251112-24-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid derivs. as retroviral protease inhibitors)

RN 251105-64-3 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S,2R)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-, [2-(1-methylethyl)-4-thiazolyl]methyl ester (9CI) (CA INDEX NAME)

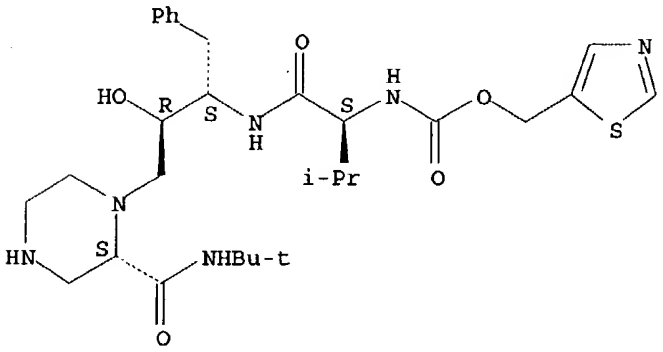
Absolute stereochemistry.



RN 251105-79-0 CAPLUS

CN Carbamic acid, [(1S)-1-[[[(1S,2R)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-, 5-thiazolylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

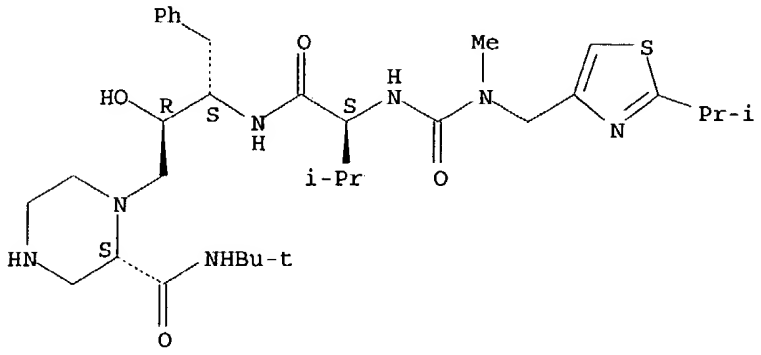


RN 251112-24-0 CAPLUS

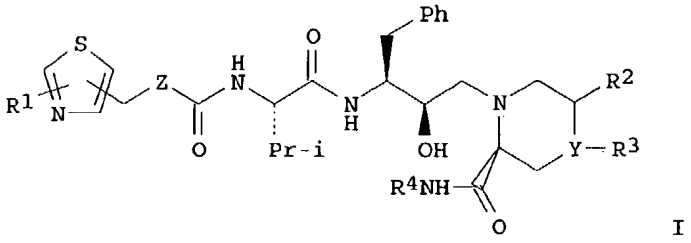
CN 2-Piperazinecarboxamide, N-(1,1-dimethylethyl)-1-[(2R,3S)-2-hydroxy-3-[[(2S)-3-methyl-2-[[[methyl[[2-(1-methylethyl)-4-

thiazolyl]methyl]amino]carbonyl]amino]-1-oxobutyl]amino]-4-phenylbutyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



I

AB Amino acid derivs. I [R1 = H, alkyl, amino, alkylamino, dialkylamino, cycloalkyl; R2 = H, R3 = -WR5, where W is (CH2)0-6, O or S; Y = N or CH (with provisos) and R5 = alkyl or aryl; or R2R3 = (CH2)4; R4 = H, alkyl, cycloalkyl, aryl, (aryl)alkyl, heterocyclyl, (heterocyclyl)alkyl, heteroaryl, or (heteroaryl)alkyl; Z = O, S, CH2, (un)substituted imino] were prepared as retroviral proteases inhibitors, in particular for inhibiting human immunodeficiency virus (HIV) protease. Thus, 2-(1-methylethyl)-4-thiazolylmethyl [(1S)-1-[[[(1S,2R)-3-[(2S)-4-(1,3-benzodioxol-5-ylmethyl)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]carbamate was prepared and showed 60% inhibition of HIV protease at 0.5 nM concentration

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

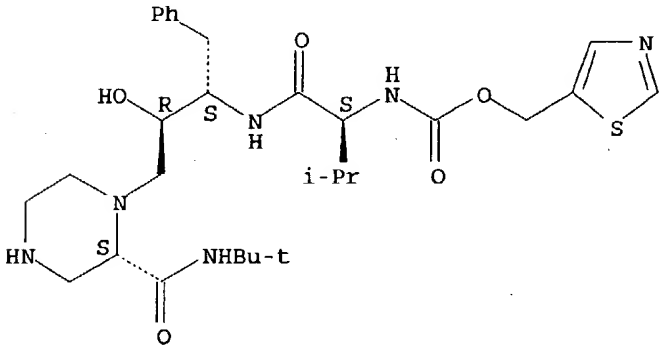
L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:753234 CAPLUS
DN 132:3551
TI Preparation of amino acid derivatives as retroviral protease inhibitors
IN Chen, Xiaoqi; Kempf, Dale J.; Norbeck, Daniel W.; Mohammadi, Fariborz
PA Abbott Laboratories, USA
SO PCT Int. Appl., 81 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9959994	A1	19991125	WO 1999-US10130	19990507
W: CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
			US 1998-80028 A	19980515
CA 2331756	AA	19991125	CA 1999-2331756	19990507
			US 1998-80028 A	19980515
			WO 1999-US10130W	19990507
EP 1077977	A1	20010228	EP 1999-920411	19990507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
			US 1998-80028 A	19980515
			WO 1999-US10130W	19990507
JP 2002515501	T2	20020528	JP 2000-549612	19990507
			US 1998-80028 A	19980515
			WO 1999-US10130W	19990507

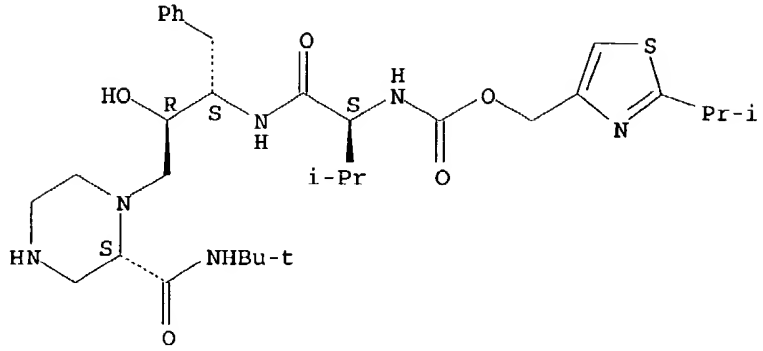
OS MARPAT 132:3551
IT **251105-79-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid derivs. as retroviral protease inhibitors)
RN 251105-79-0 CAPLUS
CN Carbamic acid, [(1S)-1-[[[(1S,2R)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-, 5-thiazolylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



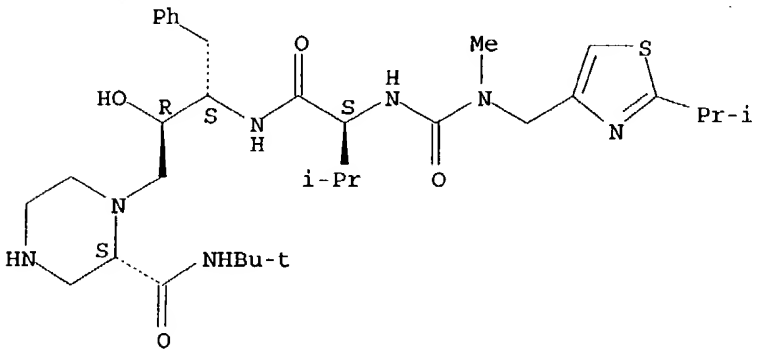
IT **251105-64-3P 251112-24-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of amino acid derivs. as retroviral protease inhibitors)
RN 251105-64-3 CAPLUS
CN Carbamic acid, [(1S)-1-[[[(1S,2R)-3-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]-, [2-(1-methylethyl)-4-thiazolyl]methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

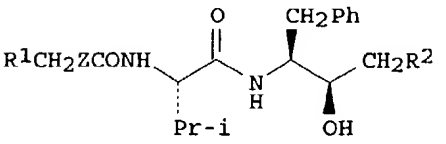


RN 251112-24-0 CAPLUS
CN 2-Piperazinecarboxamide, N-(1,1-dimethylethyl)-1-[(2R,3S)-2-hydroxy-3-[[(2S)-3-methyl-2-[[[methyl[[2-(1-methylethyl)-4-thiazolyl]methyl]amino]carbonyl]amino]-1-oxobutyl]amino]-4-phenylbutyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



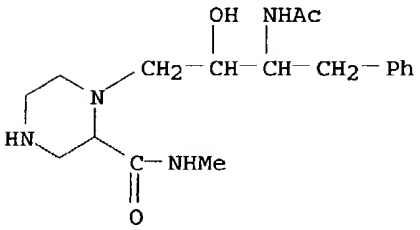
I

AB Compds. I [R1 = thiazolyl or alkyl-, amino-, alkylamino, dialkylamino, or cycloalkyl-substituted thiazolyl; R2 = 4-substituted 2-(un)substituted carbamoylpiperidino or -piperazin-1-yl; Z = O, S, CH2, NR7, where R7 = H or (un)substituted alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl] were prepared as inhibitors of retroviral proteases, in particular human immunodeficiency virus (HIV) protease. Thus, 2-(1-methylethyl)-4-thiazolylmethyl [(1S)-1-[[[(1S,2R)-3-[(2S)-4-(1,3-benzodioxol-5-ylmethyl)-2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-

(phenylmethyl)propyl]amino]carbonyl]-2-methylpropyl]carbamate was prepared and assayed for inhibition of HIV protease (60% at 0.5 nM) and antiviral activity (EC50 = 3 nM and LC50 = 12.76 μM).

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:476011 CAPLUS
DN 125:184889
TI The design, modeling and evaluation of potential HIV protease inhibitors using BLITZ, an interactive computer graphics working tool
AU Mahmoudian, M.; Laczkowski, A.; Karrer, A.; Swanson, S. M.; Meyer, E. F. Jr.
CS Department of Pharmacology, University of Medical Sciences, Teheran, Iran
SO Journal of Sciences, Islamic Republic of Iran (1996), 7(1), 8-12
CODEN: JSIIEN; ISSN: 1016-1104
PB National Center for Scientific Research
DT Journal
LA English
IT **180911-02-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design and modeling and evaluation of potential HIV protease inhibitors using interactive computer graphics working tool BLITZ in relation to AIDS treatment)
RN 180911-02-8 CAPLUS
CN 2-Piperazinecarboxamide, 1-[3-(acetylamino)-2-hydroxy-4-phenylbutyl]-N-methyl- (9CI) (CA INDEX NAME)



AB Several nonpeptide small mols. were designed as potential inhibitors of HIV protease and their structures were constructed by computer-aided mol. modeling and docked into the active site of HIV protease. Models of the complexes of inhibitors and the HIV protease were refined using nonbonded and H-bonding terms. The refined energy of selected complexes showed that the designed inhibitors fitted tightly into the active site of receptor cavity. The structure of the designed inhibitor (HI-082) was superimposed on the mol. of haloperidol (which has been reported to have anti-HIV protease activity) and it was found that they share a number of common structural features. These results showed that these small nonpeptide mols. interact strongly with the HIV protease and may therefore inhibit its action in which case they would be potential anti-AIDS agents.

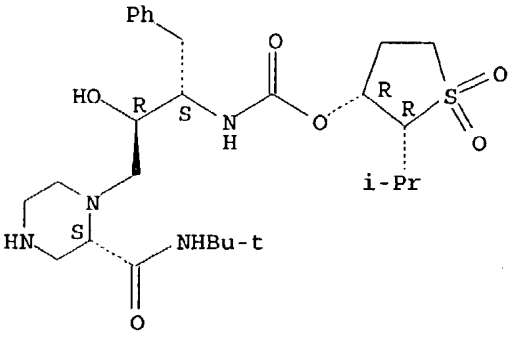
L3 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:367737 CAPLUS
DN 125:58548
TI Piperazinecarboxamide derivative HIV protease inhibitors useful for the

treatment of AIDS
IN Kim, Byeong Moon; Vacca, Joseph P.
PA Merck and Co., Inc., USA
SO Brit. UK Pat. Appl., 53 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

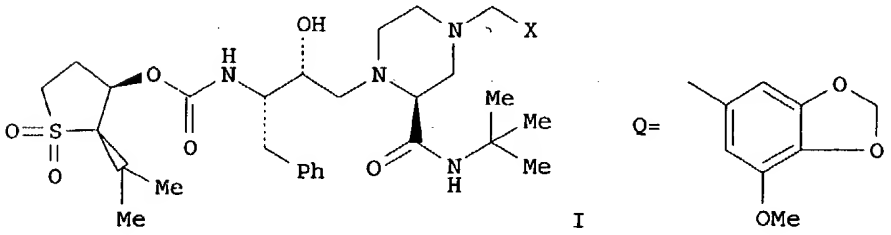
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2292146	A1	19960214	GB 1995-15802	19950801
			US 1994-289477	19940811
US 5650412	A	19970722	US 1995-548415	19951026
			US 1994-289477	19940811

OS MARPAT 125:58548
IT **165879-79-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperazinecarboxamide derivs. as HIV protease inhibitors)
RN 165879-79-8 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-1,1-dioxido-3-thienyl ester, [2R-[2α,3α[1S*,2R*,3(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



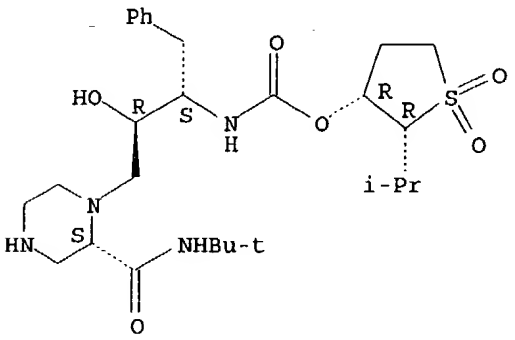
GI



AB Title compds. I [X = stable 8- to 10-membered bicyclic heterocycle, any ring of which may be saturated or unsatd., and which consists of C atoms and 1-3 heteroatoms selected from N, S, and O, with said heterocycle (un)substituted with OH, halo, C1-4 alkyl, C1-4 alkoxy, or oxo; with proviso that X ≠ thieno[2,3-b]thien-2-yl or quinolinyl], and pharmaceutically acceptable salts thereof, are useful as HIV protease inhibitors. For example, the preferred compound I [X = Q] (II) was prepared in 68% yield by reductive alkylation of the corresponding piperazine derivative [multi-step preparation given] with 3-methoxy-4,5-methylenedioxybenzaldehyde and NaBH(OAc3). In a cell-spread assay using MT-4 lymphoid cells infected with wild-type HIV-1, II had CIC95 of 25 nM.

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:857593 CAPLUS
DN 124:86938
TI Substituted alkylpyridines as P3' ligands for the hydroxyethylpiperazine class of HIV-1 protease inhibitors: improved pharmacokinetic profiles
AU Kim, B. Moon; Hanifin, Colleen M.; Zartman, C. Blair; Vacca, Joseph P.; Michelson, Stuart R.; Lin, Jiunn H.; Chen, I.-W.; Vastag, Kari; Darke, Paul L.; et al.
CS Department of Medical Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (1995), 5(19), 2239-44
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
IT **165879-79-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
{[[[(alkylamino)carbonyl]piperazinyl]hydroxyalkyl]carbamic acid thienyl ester S,S-dioxide derivs. as HIV inhibitors)
RN 165879-79-8 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-1,1-dioxido-3-thienyl ester, [2R-[2α,3α[1S*,2R*,3(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB As a systematic approach to develop HIV-1 protease inhibitors exhibiting desirable pharmacokinetic profiles, hydroxyethylpiperazine series of inhibitors containing various mono- or dialkyl-substituted pyridylmethyl groups have been examined Very high enzyme inhibitory potency and antiviral

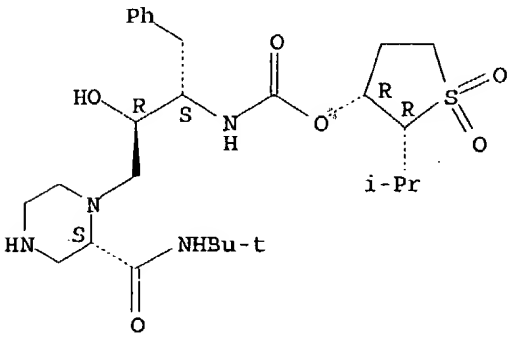
activity in a whole cell assay were observed with these inhibitors and, when administered orally to dogs, selected compds. in this series exhibited prolonged half-lives compared to the non-substituted pyridylmethyl compound, i.e., [2R-[2α,3α[1S*,2R*,3(S*)]]]-[3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(4-pyridinylmethyl)-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]carbamic acid tetrahydro-2-(1-methylethyl)-3-thienyl ester S,S-dioxide.

L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:711972 CAPLUS
DN 123:112077
TI Preparation of piperazine derivatives as HIV protease inhibitors
IN Kim, Byeong Moon; Vacca, Joseph P.; Ghosh, Arun K.; Guare, James P., Jr.; Huff, Joel R.; Hungate, Randall W.; Lee, Hee Yoon; Thompson, Wayne J.
PA Merck and Co., Inc., USA
SO PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9418192	A1	19940818	WO 1994-US1370	19940207
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
			US 1993-17090	19930212
AU 9461352	A1	19940829	AU 1994-61352	19940207
			US 1993-17090	19930212
			WO 1994-US1370	19940207

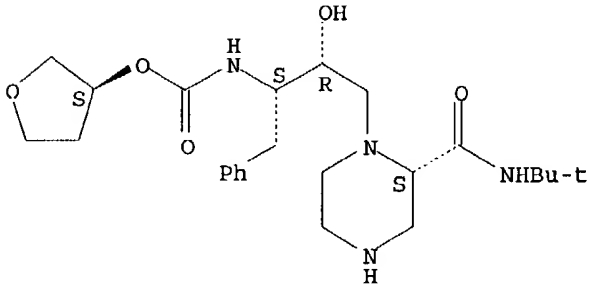
OS MARPAT 123:112077
IT **165879-79-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine derivs. as HIV protease inhibitors)
RN 165879-79-8 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-1,1-dioxido-3-thienyl ester, [2R-[2α,3α[1S*,2R*,3(S*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

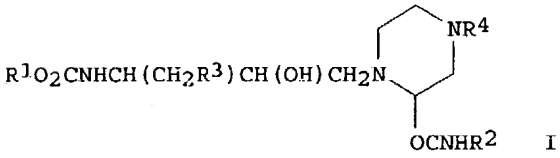


IT **159462-59-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazine derivs. as HIV protease inhibitors)
RN 159462-59-6 CAPLUS
CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-3-furanyl ester, [2S-[1[1R*(R*),2S*],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



I

AB Title compds. I (R1 = 5-7-membered carbocyclyl, 5-7-membered heterocyclyl; R2 = C1-5 alkyl, 5-7-membered carbocyclyl; R3 = Ph, C5-7 cycloalkyl; R4 = CO2, SO3, 5-7-membered heterocyclyl, C1-4 alkenyl, C3-5 cycloalkyl, etc.) or a salt thereof, useful for treating infection of HIV and AIDS, are prepared To N-tert-butyl-1-[3'(S)-[3"(S)-tetrahydrofuranyloxycarbonylamino]-2'-(R)-hydroxy-4'-phenylbutyl]piperazine-2(S)-carboxamide and 3-hydroxybenzaldehyde in MeOH were added NaBH3CN and AcOH to give title compound N-tert-butyl1-[3'(S)-[3"(S)-tetrahydrofuranyloxycarbonylamino]-2'(R)-hydroxy-4'-phenylbutyl]-4-(3'-hydroxyphenylmethyl)piperazine-2(S)-carboxamide which inhibited microbial expressed HIV protease with IC50 0.1-10 nM.

L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:120890 CAPLUS
DN 122:150813
TI A new hydroxyethylamine class of HIV-1 protease inhibitors with high antiviral potency and oral bioavailability
AU Kim, B. Moon; Vacca, Joseph P.; Guare, James P.; Hanifin, Colleen; Michelson, Stuart R.; Darke, Paul L.; Zugay, Joan A.; Emini, Emilio A.; Schleif, William; et al.
CS Dep. Medicinal Chem., Merck Research Labs., West Point, PA, 19486, USA
SO Bioorganic & Medicinal Chemistry Letters (1994), 4(19), 2273-8
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal

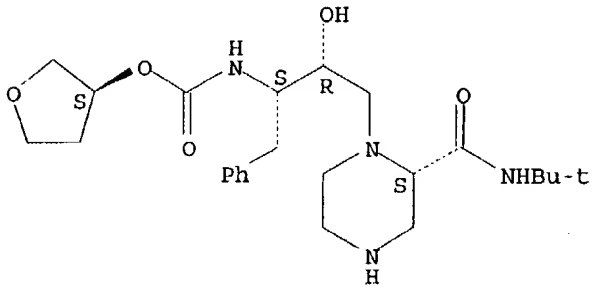
LA English

IT **159462-59-6P 159462-81-4P 159462-82-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(structure of hydroxyethylamine class of HIV-1 protease inhibitors with high antiviral potency and oral bioavailability)

RN 159462-59-6 CAPLUS

CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-3-furanyl ester, [2S-[1[1R*(R*),2S*],2R*]]- (9CI) (CA INDEX NAME)

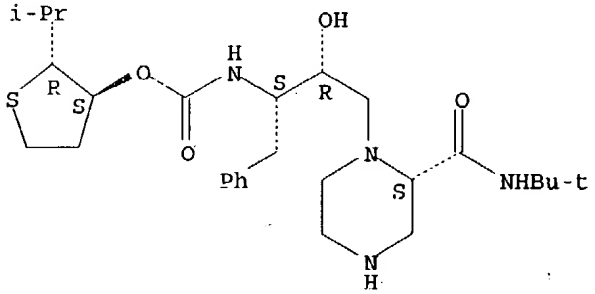
Absolute stereochemistry.



RN 159462-81-4 CAPLUS

CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-3-thienyl ester, [2R-[2α,3β[1S*,2R*(S*)]]]- (9CI) (CA INDEX NAME)

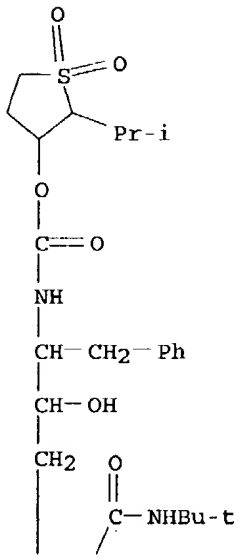
Absolute stereochemistry.



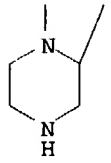
RN 159462-82-5 CAPLUS

CN Carbamic acid, [3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]-, tetrahydro-2-(1-methylethyl)-1,1-dioxido-3-thienyl ester, [2R-[2α,3β[1S*,2R*,3(S*)]]]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



AB A new hydroxyethylamine class of inhibitors was designed combining features from a clin. candidate, L-735524, along with small heterocyclic P2-ligands developed in these labs and their structure-activity relationship was studied.. Highly potent protease inhibitors possessing subnanomolar IC50's have been identified, which exhibit good antiviral potency against HIV-1 in cell culture. L-738872, a representative inhibitor in this class, showed 34% oral bioavailability in dogs.

L3 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:441332 CAPLUS
DN 113:41332
TI Preparation of peptide amides as human immunodeficiency virus inhibitors
IN Handa, Balraj Krishan; Machin, Peter James; Martin, Joseph Armstrong; Redshaw, Sally; Thomas, Gareth John
PA Hoffmann-La Roche, F., und Co. A.-G., Switz.
SO Eur. Pat. Appl., 69 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 346847	A2	19891220	EP 1989-110717	19890613
	EP 346847	A3	19911023		
	EP 346847	B1	19940511		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
				GB 1988-13940 A	19880613
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	US 5157041	A	19921020	US 1989-362621	19890605
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
	ZA 8904285	A	19900228	ZA 1989-4285	19890606
				GB 1988-13940 A	19880613
	AU 8936130	A1	19891214	AU 1989-36130	19890607
	AU 624144	B2	19920604		
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				GB 1989-8035 A	19890410
	HU 51254	A2	19900428	HU 1989-2903	19890607
	HU 205898	B	19920728		
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	DK 8902863	A	19891214	DK 1989-2863	19890612
	DK 172747	B1	19990628		
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				GB 1989-8035 A	19890410
	NO 8902407	A	19891214	NO 1989-2407	19890612
	NO 175715	B	19940815		
	NO 175715	C	19941123		
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				GB 1989-8035 A	19890410
	JP 02042048	A2	19900213	JP 1989-149265	19890612
	JP 2515019	B2	19960710		
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				GB 1989-8035 A	19890410
	KR 9705905	B1	19970422	KR 1989-8040	19890612
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	FI 8902881	A	19891214	FI 1989-2881	19890613
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	FI 95693	C	19960311		
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				GB 1989-8035 A	19890410
	AT 105549	E	19940515	AT 1989-110717	19890613
				GB 1988-13940 A	19880613
				GB 1989-8035 A	19890410
				EP 1989-110717 A	19890613
	ES 2052815	T3	19940716	ES 1989-110717	19890613
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				GB 1989-8035 A	19890410
	US 5446161	A	19950829	US 1992-916812	19920720
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				US 1989-362621 A3	19890605
	US 5554756	A	19960910	US 1995-391380	19950217
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				GB 1989-8035 A	19890410
				US 1989-362621 A3	19890605
				US 1992-916812 A3	19920720
	US 5652369	A	19970729	US 1995-394523	19950406

				GB 1988-13940 A 19880613
				GB 1989-8035 A 19890410
				US 1989-362621 A319890605
				US 1992-916812 A319920720
	US 5620987	A	19970415	US 1995-398478 19950410
				GB 1988-13940 A 19880613
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				US 1989-362621 A319890605
				US 1992-916812 A319920720

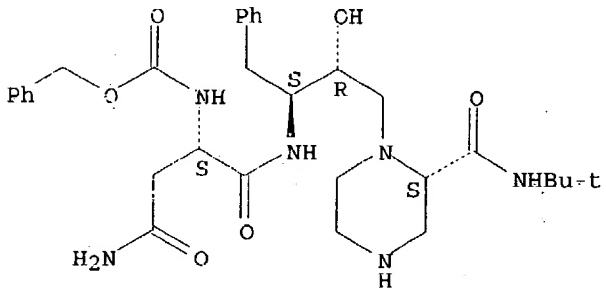
OS MARPAT 113:41332

IT **128019-64-7P 128111-43-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as HIV protease inhibitor)

RN 128019-64-7 CAPLUS

CN Carbamic acid, [3-amino-1-[[[3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-3-oxopropyl]-, phenylmethyl ester, monohydrochloride, [2S-[1[1R*(R*),2S*],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

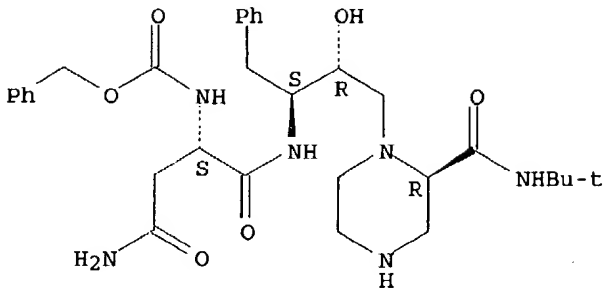


● HCl

RN 128111-43-3 CAPLUS

CN Carbamic acid, [3-amino-1-[[[3-[2-[[(1,1-dimethylethyl)amino]carbonyl]-1-piperazinyl]-2-hydroxy-1-(phenylmethyl)propyl]amino]carbonyl]-3-oxopropyl]-, phenylmethyl ester, monohydrochloride, [2R-[1[1S*(S*),2R*],2R*]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

AB R1R2NCHR3CONHCHR4CR5R6CH2N(:O)nR7CHR8R9 [I; R1 = alkoxycarbonyl, aralkoxycarbonyl, (ar)alkanoyl, cycloalkylcarbonyl, aroyl, heterocyclylcarbonyl, alkylsulfonyl, etc.; R2 = H; R1R2N = cyclic aromatic imide; R3 = (cyclo)alkyl, (aryl)alkyl, aryl, heterocyclylalkyl, cyanoalkyl, etc; R4 = alkyl, cycloalkyl(alkyl), aryl(alkyl); R5 = H; R6 = OH; R5R6 = :O; R7R8 = (un)substituted (CH2)3, (CH2)4, with 1 CH2 optionally replaced by NH, N(acyl), S, etc., optionally carrying 1 fused cycloalkane or (hetero)aromatic ring; R9 = alkoxycarbonyl, monoalkylcarbamoyl, CONHCHR10CONHR11; R10, R11 = alkyl; n = 0, 1] and their pharmaceutically acceptable salts were prepared, e.g., by coupling amines H2NCHR4CR5R6CH2NR7CHR8R9 with acids R1R2NCHR3CO2H. Thus, N1-isobutyl-L-isoleucylamide (preparation given) was coupled with Z-proline succinimide ester (Z = benzyloxycarbonyl), the resulting dipeptide was deprotected and coupled with (Z-phenylalanyl)methyl bromide, the intermediate tripeptide reduced by NaBH4 in EtOH, deprotected, and coupled with Z-Asn-OH to give N2-[N-[3(S)-[(Z-asparaginyl)amino]-2(R,S)-hydroxy-4-phenylbutyl]-L-prolyl]-N1-isobutyl-L-isoleucylamide. One (unspecified) of 2 isomers of the latter in vitro inhibited human immunodeficiency virus protease with an IC50 of 0.13 μM. IC50 values reported for 7 other I ranged from 0.01-0.87 μM.

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=> s alzheimer and piperazine
L4 234 ALZHEIMER AND PIPERAZINE

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=> s l4 and preventing
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L8   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:356443  CAPLUS
DN   138:368916
TI   Preparation of heteroarylamines as glycogen synthase kinase 3beta
     inhibitors
IN   Freyne, Eddy Jean Edgard; Buijnsters, Peter Jacobus Johannes Antonius;
     Willems, Marc; Embrechts, Werner Constant Johan; Love, Christopher John;
     Janssen, Paul Adriaan Jan; Lewi, Paulus Joannes; Heeres, Jan; De Jonge,
     Marc Rene; Koymans, Lucien Maria Henricus; Vinkers, Hendrik Maarten; Van
     Aken Koen, Jeanne Alfons; Diels, Gaston Stanislas Marcella
PA   Janssen Pharmaceutica N.V., Belg.
SO   PCT Int. Appl., 88 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
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PI   WO 2003037891      A1    20030508      WO 2002-EP12077  20021029
     WO 2003037891      C1    20030904
          W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
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                                          EP 2001-204196 A 20011101
OS   MARPAT 138:368916
GI
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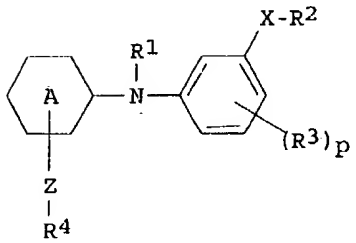

I

AB This invention concerns compds. of formula (I), N-oxides, pharmaceutically acceptable addition salts, quaternary amines and stereochem. isomeric forms thereof [wherein ring A = pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl; R1 = H, aryl, formyl, C1-6 alkylcarbonyl, C1-6 alkyl, formyl-C1-6 alkyl, C1-6 alkyloxycarbonyl, C1-6 alkylcarbonyloxy, C1-6 alkyloxy-C1-6 alkylcarbonyl optionally substituted with C1-6 alkyloxycarbonyl; X, Z = a direct bond or a linker atom or group; R2 = H, each (un)substituted C1-10 alkyl, C2-10alkenyl, C2-10 alkynyl, or carbocycle or heterocycle group; R3 = H, HO, halo, each optionally substituted C1-6 alkyl, C1-6 alkenyl, or C2-6alkynyl, C1-6 alkyloxy, C1-6 alkylthio, C1-6 alkyloxycarbonyl, C1-6 alkylcarbonyloxy, CO2H, cyano, nitro, amino, mono- or di(C1-6 alkyl)amino, polyhalo-C1-6 alkyl, polyhalo-C1-6 alkyloxy, polyhalo-C1-6 alkylthio, R21, R21-C1-6 alkyl, R21O, R21S, R21CO, R21S(O)n, R21S(O)nNH, NHCHO, CONHNH2, R21CONH, C(:NH)R21, etc.; wherein n = 1,2; R21 = each (un)substituted saturated, partially saturated, or aromatic mono-, di-, or tricyclic carbocycle or heterocycle group; R4 = (un)substituted saturated, partially saturated, or aromatic mono-, di-, or tricyclic carbocycle or heterocycle provided that -X-R2 and/or R3 is other than hydrogen; p = 1-3]. These compds. are useful for the **prevention** or the treatment of **diseases** mediated through glycogen synthase kinase 3β (GSK3β) including bipolar disorder (in particular manic depression), diabetes, **Alzheimer**'s **disease**, leukopenia, FTDP-17 (fronto-temporal dementia associated with Parkinson's **disease**), cortico-basal degeneration, progressive supranuclear palsy, multiple system atrophy, Pick's **disease**, Niemann Pick's **disease** type C, dementia pugilistica, dementia with tangles only, dementia with tangles and calcification, Down syndrome, myotonic dystrophy, Parkinsonism-dementia complex of Guam, AIDS related dementia, postencephalic Parkinsonism, prion **diseases** with tangles, subacute sclerosing panencephalitis, frontal lobe degeneration (FLD), argyrophilic grains **disease**, subacute sclerotizing panencephalitis (SSPE) (late complication of viral infections in the central nervous system), inflammatory **diseases**, cancer, dermatol. disorders, neuronal damage, schizophrenia, and pain. Thus, a mixture of 0.002 mol 2-[(4-cyano-3-benzyloxyphenyl)amino]pyrimidine-4-carboxylic acid Et ester and 0.002 mol **piperazine** in 15 mL MeOH was stirred at room temperature for 1 day to give 0.32 g N-[2-[(4-cyano-3-benzyloxyphenyl)amino]pyrimidin-4-ylcarbonyl] **piperazine** (II). II and 2-(1,3-benzodioxol-5-ylamino)-4-(2,4,6-trimethylphenylamino)pyrimidine showed pIC50 of 5.53 and 5.30, resp., against GSK3β.

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:977659 CAPLUS
DN 138:205081
TI Preparation of aminoacylpiperazines and -piperidines for promoting neuronal repair or **preventing** neuronal damage.
IN Lauffer, David; Tomlinson, Ronald; Ottow, Eckard; Botfield, Martyn
PA Vertex Pharmaceuticals Incorporated, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2002102381 A1 20021227 WO 2002-US18999 20020613
WO 2002102381 C2 20030306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2001-298328PP 20010614
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OS MARPAT 138:205081

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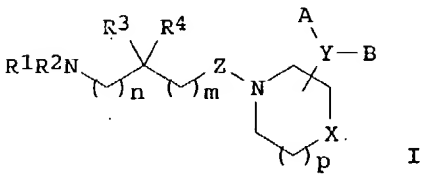

I

AB Title compds. [I; R1-R4 = (O-, S-, SO-, SO2-, CO-, NR5-interrupted) alkyl, aralkyl, alkenyl, alkynyl, aralkenyl, aralkynyl; R1R2, R3R4 = atoms to form (aryl-fused) 4-7 membered rings; m, n = 0, 1; X = C(R5)2, NR5, N, O, S, SO, SO2; Y = bond, (O-, S-, SO-, SO2-, CO-, NR5-interrupted) alkyl, alkenyl, alkynyl; Z = CO, CH2; p = 0-2; A, B = H, aryl; 2 C atoms in the ring containing X and N may be linked via an alkylene or alkenylene moiety], were prepared Thus, N-benzyl-N-methylalanine, diisopropylethylamine, and pivaloyl chloride were stirred 2 h in CH2Cl2; 1-(4-fluorophenyl) **piperazine** in CH2Cl2 was added dropwise followed by stirring for 24 h to give 2-(benzylmethylamino)-1-[4-(4-fluorophenyl)-piperazin-1-yl]propan-1-one.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:849594 CAPLUS
DN 137:353065
TI Preparation of 4-heterocyclylquinoline derivatives as beta-amyloid precursor protein secretion promoters
IN Kakihana, Mitsuru; Kato, Kaneyoshi; Mori, Masaaki; Yamashita, Toshiro
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 233 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002088087	A1	20021107	WO 2002-JP4148	20020425

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

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CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
JP 2001-128677 A 20010426
JP 2002-43523 A 20020220
JP 2003313167 A2 20031106 JP 2002-124873 20020425
JP 2001-128677 A 20010426
JP 2002-43523 A 20020220
EP 1382598 A1 20040121 EP 2002-722787 20020425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2001-128677 A 20010426
JP 2002-43523 A 20020220
WO 2002-JP4148 W 20020425

OS MARPAT 137:353065

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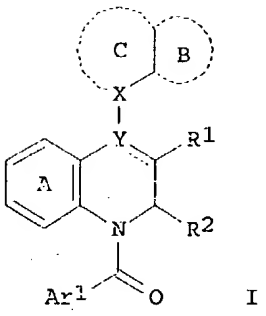

I

AB Novel compds. represented by the following general formula (I), salts thereof or prodrugs of the same [wherein R1, R2 = H, (un)substituted lower alkyl or HO; or R1 and R2 together with the C atom attached to them form a 4 to 7-membered ring; A1 = (un)substituted aromatic group; the ring A = (un)substituted benzene ring; the ring B = (un)substituted aromatic ring; the ring C = (un)substituted 4- to 8-membered ring which may be fused with an optionally substituted ring; X = CH or N; the solid line accompanied by a dotted line represents a single or double bond; when it represent a single bond, Y is CH or N; when it represents a double bond, it is C] are prepared These compds. provide soluble beta-amyloid precursor protein (soluble βAPP, sAPP) secretion promoters and/or apoptosis inhibitors which are efficacious in **preventing** and/or treating neurodegenerative **diseases** such as **Alzheimer's disease**, Parkinson's **disease**, neuropathy, and senile dementia and nerve cell damages at cerebrovascular disorders. Thus, iodotrimethylsilane was added to a solution of cis-1-(3,4-dimethoxybenzoyl)-2-methyl-1,2,3,4-tetrahydro-4-quinolinol in CHCl3 under ice-cooling, stirred for 2 h, concentrated, dissolved in THF, and stirred with 1,2,3,4-tetrahydroquinoline and BaCO3 at room temperature for 48 h to give cis-4-(1,2,3,4-tetrahydroquinolin-1-yl)-1-(3,4-dimethoxybenzoyl)-1,2,3,4-tetrahydroquinoline (II). II was separated by HPLC on a CHIRALPAK AD column to give (+)- and (-)-II. (-)-II at 10 nM increased the secretion of sAPP by .apprx.2.2 fold in rat

pheochromocytoma PC12h cell line and completely inhibited the apoptosis of PC12h cell caused by the glutamic acid-induced inhibition of the uptake of glutathione.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:754196 CAPLUS
DN 137:257677
TI Methods of treating or **preventing Alzheimer**'s **disease** using 4-aryl-3-aralkoxypiperidines and -azabicyclooctanes
IN Nieman, James A.; Fang, Lawrence; Jagodzinska, Barbara
PA Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SO PCT Int. Appl., 449 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002076440	A2	20021003	WO 2002-US9100	20020321
WO 2002076440	A3	20021128		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-278371PP 20010323
US 2001-308729PP 20010730

OS MARPAT 137:257677
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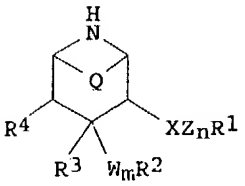

I

AB Disclosed are methods for treating or **preventing Alzheimer**'s **disease**, and other **diseases**, and/or inhibiting β-secretase enzyme, and/or inhibiting deposition of A beta peptide in a mammal, using 3,4-disubstituted piperidinyl compds. (I) wherein the variables R1, R2, R3, R4, Q, W, X, Z, m, and n are defined below. Although neither the compds. nor the methods of preparation are claimed, .apprx.150 example prepns., translations from the German examples of patent WO 9709311, are included. I inhibit β-secretase with IC50 < 50 μM; compds. that are effective inhibitors of β-secretase activity demonstrate reduced cleavage of the substrate as compared to a control. In I, R1 is aryl, heterocycle; R2 is Ph, naphthyl, acenaphthyl,